Author's response to reviews

Title: Effect of leisure time physical activity on severe knee or hip osteoarthritis leading to total joint replacement: a population-based prospective cohort study

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Author's response to reviews: see over
Dear Editor,

Thank you for your response and for the reviewers’ valuable comments and constructive criticism. Changes have been made in order to meet the criticism raised, and in cases where we have not made the suggested changes, our reasons for not doing so are given.

We hereby submit the revised version of the paper, with marked changes, for consideration regarding publication along with response to each of the specific comments provided by the reviewers.

Sincerely,

Eva Ageberg
Reviewer's report

Title: Effect of leisure time physical activity on severe knee or hip osteoarthritis leading to total joint replacement: a population-based prospective cohort study

Version: 1 Date: 13 January 2012
Reviewer: Jennifer Hootman
Reviewer's report: Major Compulsory Revisions

COMMENT

1. Leisure-time physical activity measurement. Reference #14 refers to the original paper on the MLTPA questionnaire. It is unclear exactly how the original instrument was modified and if its reliability and validity had been established. It seemed like there were significant modifications of the MLTPA such as the original instrument asked 64 different activities versus 18 in the modified and the modified version asked about activities during 4 seasons versus the original asks them for each of the 12 months. Looking at reference #15 also does not explain how and why the valid and reliable MLTPA was modified. Although there is a small reference to what seems to be a reliability/reproducibility coefficient, it was done only with persons reporting exceptionally high rates of physical activity in the baseline survey and it is unclear the time period between the 2 administrations. The reader needs more information on the psychometrics of this physical activity measure. There is also a vague reference to validity mentioned in discussion paragraph #10. But I think this information should be moved up to the methods section and more details provided on the reliability and validity of the modified questionnaire.

AUTHORS’ RESPONSE AND ACTION

More information on the questionnaire and limitations associated with the questionnaire are now provided in the method and discussion sections (see pasted below).

Methods:

“Leisure time physical activity

At baseline, leisure time physical activity was assessed as described [14]. A questionnaire, adapted from the Minnesota Leisure Time Physical Activity Questionnaire, was used [15]. The participants were asked to fill in how many minutes per week they spent on each of 18 different activities during each of the four seasons. Each activity was multiplied by an activity-specific factor, representing assumed energy consumption (e.g., the factor for ball sports was higher than that for walking). All activities for each individual were then added together, creating an overall leisure time physical activity score. Thus, this score, represents the aggregated assumed energy consumption, taking both duration and intensity of physical activities into account [16]. The score was divided into quartiles: low (Q1), low–moderate (Q2), moderate–high (Q3), and high physical activity (Q4). The questionnaire showed acceptable validity, equal to that of a 3-point scale of physical activity (low, moderate, high), compared with accelerometry [17]. Reproducibility, assessed by telephone interview in the sample reporting the highest physical activity, was high (93%) [16].

Discussion:

“Self-report surveys to measure physical activity are associated with some limitations, such as, over-reporting, reduced accuracy for moderate physical activity, and moderate reproducibility [3]. Accelerometry provides an objective and reliable measure of the frequency, duration and intensity of physical activity, but is impractical to use in large cohorts.
Although validity and reliability were reported for the questionnaire used [16, 17], these studies were small, and further validation may be required.

**COMMENT**

2. The measure of leisure-time PA does take into account the frequency, duration and intensity of the activity, the intensity is based on the cardio-respiratory effects (I assume some type of MET value was used for intensity) and does not take into account the joint loading forces of the activity. For example, running 4.0 mph is a 6.0 MET activity and swimming at moderate effort is a 5.8 MET activity. These 2 activities have similar MET values (e.g., energy expenditure) but the forces subjected to the knee joint are very different. While there is no standardized compendium for joint loading forces as there is for MET values, there have been several attempts at capturing joint loading in the PA exposure in the arthritis and bone literature. I suggest that the authors consider some type of analysis that takes into account joint loading. This could be as simple as doing subanalyses of persons only reporting low (e.g., walking, swimming, cycling), moderate (lawn and garden) and high (downhill skiing, soccer, etc.) joint loading activities. Or they may consider using one of the methods reported in the literature or make their own joint loading index variable that can be used to adjust the regression models. They speak vaguely to this issue in discussion paragraph #11, but I suggest bringing in the studies that have attempted to include joint loading in their measure of PA exposure.

Two examples of methods used to "weight" PA data according to joint loading forces are already in your reference list. References # 24 and #29. There are other studies from the bone literature that have attempted to create "bone loading units" too.

**AUTHORS’ RESPONSE**

It may be questioned whether the questionnaire that we used is sufficiently evaluated regarding validity and reliability. This is now included in the discussion (see response to previous comment). Another limitation is that duration and intensity of physical activity is taken into account, but not joint loading. This is true also for other questionnaires within the field of OA (last paragraph in the discussion section). As you point out, there is to date no standardized compendium for joint loading forces as there is for MET values. We believe that if we attempt to create a new set for joint loading from our available data, this may leave us with an unreliable outcome. For these reasons, we have made no attempt to include joint loading in the physical activity score.

**Minor Essential Revisions**

**COMMENT**

1. Definitions of knee and hip OA:
   a. hip OA was defined as the first hip replacement with a comcomitant diagnosis of OA. However, someone could have had an OA diagnosis, but actually had a hip replacement due to a hip fracture and not necessarily due to end-stage hip OA. Can you clarify if hip replacements due to fracture were excluded?
AUTHORS’ RESPONSE AND ACTION

We have clarified this so that it reads: “Knee OA was defined as a first knee replacement or high tibial osteotomy in combination with a concomitant diagnosis of OA, and hip OA was defined as a first hip replacement in combination with a concomitant diagnosis of OA [16]. That is, the surgery indication was OA, and all other diagnoses and indications were excluded.” This is also clarified throughout the paper, i.e., “knee/hip replacement due to OA”.

COMMENT

b. There is a considerable amount of time (~6 years) from the latest censor data (December 31, 2005) and now. If data are available from a hospital discharge registry regarding joint replacement, then why were additional cases not included after 2005? It seems the mortality and emigration information should also be available between 2005 and 2011.

AUTHORS’ RESPONSE

The subjects were followed over 11 years, with the final follow-up in 2005 (provided in “study population” on page 7, and also in other publications including this cohort). There may be chance to obtain data from the registry for a few more years. However, the participants will be older (mean age over 60 years), they may have changed their activity level during this time, and we believe that it is unlikely that a few more years of follow-up will influence the results. Therefore, we have decided not to make an attempt to extend the follow-up time of our study.

COMMENT

c. It seems you have the exact date of “failure” or censor because you have the date of surgery, date of death or emigration. But this should be explicitly stated as the Cox model used would not be appropriate if you have interval censored data.

AUTHORS’ RESPONSE AND ACTION

We have clarified this and it now reads: “The exact follow-up time was calculated, separately for knee and hip OA, from the baseline examination until the first OA surgery, emigration from Sweden, death or December 31 2005, whichever came first [16].”

COMMENT

2. Discussion, paragraph 3: Can you speculate the mechanisms for this protective effect among women for hip replacement? Could it be something to do with Q-angle, or the different activity patterns among women (women may choose lower impact activities)? Also, I disagree with the last sentence in this paragraph. A relative risk of 0.66 equates to a 34% lower risk. I would consider that important, particularly at the population level because OA is so prevalent.
AUTHORS’ RESPONSE AND ACTION

We have made some revision in this paragraph: “The values in the present study reached statistical significance for women, showing a 34% lower risk of hip OA in those with the highest compared with the lowest physical activity (lowest RR 0.66, lowest CI 0.48). This indicates a protective role of leisure time physical activity for the incidence of hip replacement in women. Further studies are needed to confirm this possible gender-difference.”

Because studies like ours are of exploratory character, and because of the limitations of our study, such as no information on previous joint injury or life-time physical activity (discussed further down in the manuscript), we believe that we need to be cautious in interpreting the results. Further studies are required to confirm the gender-difference that we found. Also, studies on the influence of biological factors (for example Q-angle) and factors related to physical activity (load, frequency etc) would be valuable and important. However, we believe that including such discussion in our current paper would be too speculative.

COMMENT

3. Discussion, paragraph 8: While the authors appropriately discuss the limitation that they did not control for previous injury history, this is a pretty major limitation. Do you have any data on what the most common activities that were reported by the subjects? For instance some sports like (soccer, handball, etc.) have high rates of knee injuries while walking does not. So is there a way you can expand on this limitation a little?

AUTHORS’ RESPONSE AND ACTION

We have now included analysis for the four most commonly reported activities:

Results: “The four most commonly reported activities were walking, bicycling, using stairs, and gardening. None of these activities were associated with knee replacement or osteotomy (Figure 1).” And “Walking was associated with a lower risk of hip replacement (Figure 1). This was specifically seen in women (adjusted RR 0.75 (95% CI 0.57, 0.98). The adjusted RR (95% CI) for men was 0.77 (0.54, 1.1).”

Discussion: “Walking was associated with a reduced risk for hip replacement, specifically in women. Physical activity involving higher joint loads (soccer, weight lifting), regular or intense exercise (elite, ex-athlete, physical education teachers), and frequent knee-bending activities may be associated with an increased risk for OA [1, 2, 21-24], although this risk is less than that for previous joint injury and overweight [2]. Physical activity involving lower joint loads, (long-distance running, swimming, walking, golf), and moderate exercise do not appear to increase the risk of knee or hip OA development or progression, or may even have a protective role [2, 4, 5, 8, 22, 24, 25]. Participation in sports activities, such as ball games, was not particularly common in our cohort, which is likely related to the age of the participants (mean 58 years at baseline). Therefore, comparison of activities involving high or low joint loading could not be performed.”
COMMENT

4. Discussion paragraph #12: Again, taking into account the joint loading aspects of different activities may not require a special questionnaire, but may require developing and validating "scoring mechanisms" for existing questionnaires that allow for the incorporation of the joint loading aspects of activities into the exposure measurement.

AUTHORS’ RESPONSE AND ACTION

Please see response to previous comments.

Discretionary Revisions

COMMENT

1. Background, paragraph 2: there is a second paper related to reference #7 (Cheng et al 2000) which is referenced later (ref # 29). In the follow-up paper the authors took into account joint stress related to physical activity in their exposure measurement and also controlled for previous injury which the Cheng paper did not. Suggest moving reference #29 up with reference #7.

AUTHORS’ RESPONSE AND ACTION

Changes are made according to your suggestion.

COMMENT

2. Discussion, paragraph 1, sentence 3: suggest inserting "a possible gender difference".

AUTHORS’ RESPONSE AND ACTION

Changes have been made and the sentence now reads: “The possible gender difference in effects of physical activity, denote that in men and women should be analyzed separately.”

COMMENT

3. Discussion, paragraph 4, sentence 3. I would consider joint replacement a "severe" OA outcome, so your outcomes are representing only the "tip of the iceberg".

AUTHORS’ RESPONSE

We agree that joint replacement can be an outcome of severe OA. To further clarify this, “the tip of the iceberg” is now included in this paragraph: “...A limitation of this definition is that only a small
proportion of the total OA population undergoes knee or hip replacement (“the tip of the iceberg”). However, it has the advantage of an unambiguous relationship with the OA disease burden. So, from our results, we can draw conclusions for this group only, and not for those with possible symptomatic or radiographic OA and less severe disease, or those with severe OA that for a variety of reasons (e.g., not willing to consider TJR) have not undergone joint replacement [19]. The presence and effects of such patient selection bias cannot be ruled out, but it is difficult to value whether this would cause an over- or underestimation of our results.”

COMMENT

4. Discussion, Paragraph 9: In addition to reference #17, regarding the combined high occupational with leisure activity increases the risk of knee replacement, Dr Felson's work in the Framingham Study also supports this finding for incident OA.

AUTHORS’ RESPONSE AND ACTION

This reference is included according to your suggestion: “The interplay between physical activity at work and during leisure time and the association with knee and hip OA may be important to consider in future studies. Men with high exposure to both sports activities and occupational/leisure time physical work load may have an increased risk of knee replacement due to OA [17]. It was also reported that men whose jobs included both knee bending and higher physical demands had an increased risk of radiographic incident OA (Felson, 1991).”

COMMENT

Also, I think the last sentence in this paragraph is off topic and not needed.

AUTHORS’ RESPONSE AND ACTION

The sentence is omitted according to your suggestion-

**Level of interest:** An article of importance in its field  
**Quality of written English:** Acceptable  
**Statistical review:** No, the manuscript does not need to be seen by a statistician.  
**Declaration of competing interests:** I declare that I have no competing interests.
Reviewer's report

Title: Effect of leisure time physical activity on severe knee or hip osteoarthritis leading to total joint replacement: a population-based prospective cohort study
Version: 1 Date: 22 December 2011
Reviewer: Bård Natvig

Reviewer's report:
In my opinion this is a well written and well designed study that adds to current knowledge in an important field of research. There are several limitations in the, but they are addressed properly in the discussion.

I have only minor comments, questions and suggestions:

COMMENT

1. Abstract: The RR for hip OA (0.66) could be explained (as protective effect), it is not self evident. It is stated in the conclusion, but the direction of the effect can be stated in the result abstract.

AUTHORS' RESPONSE AND ACTION

This is clarified and the sentence now reads: “For women only, the adjusted RR (95% CI) for hip OA was 0.66 (0.48, 0.89) (fourth vs. first quartile), indicating a lower risk of hip OA in those with the highest compared with the lowest physical activity.”

COMMENT

2. Leisure time physical activity: Reference 13 does not seem to be an obvious reference for assessment of leisure time physical activity? Would it be better do describe how it was assessed straightforward: ...assessed with a modified.....

AUTHORS' RESPONSE AND ACTION

More information on the questionnaire is now provided in the method section (see pasted below).

Methods:

“Leisure time physical activity

At baseline, leisure time physical activity was assessed as described [14]. A questionnaire, adapted from the Minnesota Leisure Time Physical Activity Questionnaire, was used [15]. The participants were asked to fill in how many minutes per week they spent on each of 18 different activities during each of the four seasons. Each activity was multiplied by an activity-specific factor, representing assumed energy consumption (e.g., the factor for ball sports was higher than that for walking). All activities for each individual were then added together, creating an overall leisure time physical activity score. Thus, this score, represents the aggregated assumed energy consumption, taking both duration and intensity of physical activities into account [16]. The score was divided into quartiles: low (Q1), low–moderate (Q2), moderate–high (Q3), and high physical activity (Q4). The questionnaire showed acceptable validity, equal to that of a 3-point scale of physical activity (low, moderate, high), compared with accelerometry [17]. Reproducibility, assessed by telephone interview in the sample reporting the highest physical activity, was high (93%) [16].
COMMENT

3. The figure (flow chart) with alternative n for knee and hip (with hips in brackets) could have been easier to interpret. Knee and hip should be equally important? Please consider another design, or perhaps to parallel figures?

AUTHORS’ RESPONSE AND ACTION

The Figure may be confusing to the reader, as it provides the number of cases included in the separate analyses. Therefore, we have excluded the Figure and now provide the n for knee and hip in “study population” as follows:

“The participants were followed until 2005 (Table 1). In the present report, participants who had been surgically treated due to hip or knee OA before the baseline examination were excluded (knee n=129, hip n=184).”

And in the results, for knee: “There were 27813 subjects available for the analysis of the incidence of knee OA from baseline to final follow-up, i.e., over 11 years (missing data n=507)” and hip: “There were 27760 subjects available for the analysis of the incidence of hip OA from baseline to final follow-up (missing data n=505).”

Level of interest: An article of importance in its field
Quality of written English: Acceptable
Statistical review: No, the manuscript does not need to be seen by a statistician.
Declaration of competing interests: I declare that I have no competing interest